

1           1.     A method for preparing a substrate for detecting at least one  
2     analyte in a sample comprising the steps of:  
3                 a) exposing the sample to at least two different selectivity  
4     conditions, each selectivity condition defined by the combination of an adsorbent and an  
5     eluant, to allow retention of the analyte by the adsorbent;  
6                 b) identifying by desorption spectrometry at least one selectivity  
7     condition under which the analyte is retained; and  
8                 c) preparing a substrate comprising at least one adsorbent of an  
9     identified selectivity condition.

1           2.     The method of claim 1 wherein the step of identifying comprises  
2     identifying at least one selectivity condition under which a plurality of analytes are  
3     retained.

1           3.     The method of claim 1 wherein the step of preparing comprises  
2     preparing a substrate comprising a plurality of adsorbents that retain the analyte under an  
3     elution condition as a multiplex adsorbent.

1           4.     A method for progressively identifying a selectivity condition with  
2     improved resolution for an analyte in a sample comprising the steps of:  
3                 (a) identify a selectivity condition that retains an analyte in a  
4     sample by:  
5                     (i) exposing a sample to a set of selectivity conditions, each  
6     selectivity condition defined by at least one binding characteristic and at least one elution  
7     characteristic;  
8                     (ii) detecting analyte retained under each selectivity  
9     condition by desorption spectrometry; and  
10                    (iii) identifying a selectivity condition that retains the  
11     analyte; and  
12                 (b) identifying a selectivity condition with improved resolution for  
13     the analyte by:

- 14 (i) selecting at least one binding characteristic or elution  
15 characteristic from the identified selectivity condition and adding it to a selectivity  
16 characteristic constant set;
- 17 (ii) exposing the sample to a modified set of selectivity  
18 conditions wherein each selectivity condition in the modified set comprises (1) the  
19 selectivity characteristics in the constant set and (2) a binding characteristic or elution  
20 characteristic that is not in the constant set; and
- 21 (iii) identifying a selectivity condition from the modified set  
22 by desorption spectrometry that retains the analyte with improved resolution compared  
23 with a prior identified selectivity condition.

1 5. The method of claim 4 further comprising the step of repeating step  
2 (b) at least once.

1 6. The method of claim 5 comprising repeating step (b) until a  
2 selectivity condition is identified that retains only the target analyte from the sample.

1 7. A substrate for desorption spectrometry comprising an adsorbent  
2 from a selectivity condition identified to resolve an analyte by the method of claim 4.

1 8. The substrate of claim 7 in the form of a kit further comprising an  
2 eluant from the selectivity condition or instructions on using the eluant in combination  
3 with the adsorbent.

1 9. A method for determining whether an analyte is differentially  
2 present in a first and second biological sample comprising the steps of:  
3 a) determining a first retention map for the analyte in the first  
4 sample for at least one selectivity condition;  
5 b) determining a second retention map for the analyte in the second  
6 sample for the same selectivity condition; and  
7 c) detecting a difference between the first and the second retention  
8 maps;

9                   whereby a difference in the retention maps provides a determination  
10 that the analyte is differentially present in first and second samples.

1                   10.    The method of claim 9 wherein the first biological sample derives  
2 from a healthy subject and the second biological sample is from a subject suffering from  
3 a pathological condition.

1                   11.    The method of claim 9 wherein the biological samples comprise  
2 first and second cell extracts.

1                   12.    The method of claim 9 wherein the retention map comprises a  
2 plurality of selectivity conditions.

1                   13.    The method of claim 9 comprising, before the step of detecting, the  
2 step of converting the analyte into at least one fragment whose molecular mass smaller  
3 than the mass of the analyte.

1                   14.    The method of claim 9 wherein the step of detecting a difference is  
2 performed in a programmable digital computer.

1                   15.    The method of claim 9 for determining whether an agent alters the  
2 expression of a protein in a biological sample further comprising the step of  
3 administering the agent to a first biological sample but not to a second biological sample.

1                   16.    The method of claim 10 wherein the sample is selected from the  
2 group consisting of blood, urine, serum and tissue.

1                   17.    The method of claim 10 further comprising identifying an analyte  
2 that is present in a greater amount in second biological sample than in the first biological  
3 sample, whereby the analyte is identified as a candidate diagnostic marker for the  
4 pathological condition.

1                   18.    The method of claim 11 wherein the first cell extract is derived  
2 from a healthy cell and the second cell extract is derived from a cancer cell.

1                   19.    A method of diagnosing in a subject a disease characterized by at  
2 least one diagnostic marker comprising the steps of:

3                         a) providing a substrate for use in desorption spectrometry that  
4 comprises at least one addressable location, each addressable location comprising an  
5 adsorbent that resolves at least one of the diagnostic markers under an elution condition;

6                         b) exposing the substrate to a biological sample from the subject  
7 under the elution condition to allow retention of the diagnostic marker; and

8                         c) detecting retained diagnostic marker by desorption spectrometry;  
9 whereby detecting retained diagnostic marker provides a diagnosis  
10 of the disease.

1                   20.    The method of claim 19 wherein diagnosis involves detection of a  
2 plurality of diagnostic markers and the addressable locations comprise adsorbents that  
3 resolve the plurality of diagnostic markers.

1                   21.    A kit for detecting an analyte in a sample comprising (1) a  
2 substrate for use in desorption spectrometry that comprises at least one addressable  
3 location, each addressable location comprising an adsorbent that resolves an analyte  
4 under a selectivity condition comprising the adsorbent and an eluant, and (2) the eluant  
5 or instructions for exposing the sample to the selectivity condition.

1                   22.    The kit of claim 21 for the diagnosis of a disease wherein the at  
2 least one analyte is at least one diagnostic marker for the disease.

1                   23.    The kit of claim 22 wherein the disease characterized by a plurality  
2 of diagnostic markers and the substrate comprises a plurality of addressable locations,  
3 each addressable location comprising an adsorbent that resolves at least one of the  
4 diagnostic markers.

1                   24.    The kit of claim 23 wherein at least one adsorbent is a multiplex  
2   adsorbent comprising adsorbent species that each retain at least one diagnostic marker.

1                   25.    The kit of claim 23 wherein at least one adsorbent does not  
2   comprise a biopolymer.

1                   26.    The kit of claim 23 wherein at least one addressable location  
2   comprises a ligand specific for a diagnostic marker.

1                   27.    The kit of claim 26 wherein the ligand is an antibody.

1                   28.    A substrate for desorption spectrometry comprising at least one  
2   adsorbent in at least one addressable location wherein the at least one adsorbent resolves  
3   a plurality of diagnostic markers for a pathological condition from a patient sample.

1                   29.    The substrate of claim 28 wherein at least one adsorbent does not  
2   comprise a biopolymer.

1                   30.    The substrate of claim 28 wherein one adsorbent resolves the  
2   plurality of diagnostic markers.